REMARKS

Claims 2, 5-6, 12, 37-45, and 47-51, including independent claim 37, are currently pending in the present application. As indicated above, independent claim 37 has been amended to incorporate the features of previous dependent claim 46 and specify that the porous membrane defines a calibration zone within which is immobilized a polyelectrolyte having a net charge opposite to that of and configured to bind with the detection probes, the calibration probes, or combinations thereof.

The Office Action rejected dependent claim 46 (now incorporated into independent claim 37) under *35 U.S.C. § 103(a)* as being obvious over Brooks, et al. in view of Buck and further in view of U.S. Patent No. 5,670,381 to Jou, et al. More specifically, the Office Action agreed that neither Brooks, et al. nor Buck discloses a calibration zone within which is immobilized *a polyelectrolyte having a net charge opposite* to that of and configured to bind with the detection probes, the calibration probes, or combinations thereof. Nevertheless, the Office Action cited Jou, et al. for this teaching. Respectfully, however, Applicants respectfully submit that one of ordinary skill in the art would not have found it obvious to make such a combination.

Jou, et al. describes a sandwich assay in which a soluble capture reagent can include an analyte-specific binding member that has been bound to a charged substance. In solution, the capture reagent is contacted with a test sample suspected of containing an analyte and is also contacted with an indicator reagent. The indicator reagent includes a specific binding member and a detectable label. Upon one- or two-step mixing, a binding reaction results in the formation of a capture reagent/analyte/indicator reagent complex. This complex is in solution and still in the

reaction mixture. The assay also includes the step of separation of the complex from the reaction mixture by using a solid phase that is either oppositely charged with respect to the capture reagent (i.e., the charged substance of the capture reagent) or that retains a second oppositely charged substance. (Col. 22, ll. 29-62.) The assay can be performed in a porous solid phase material (col. 24, ll. 52-54). The porous material can include a reaction zone containing the second charged substance such that the capture reagent and complexes thereof are immobilized in the reaction zone by the interaction of the two oppositely charged substances (col. 6, ll. 32-37). One of the major advancements of the assay is the use of liquid phase kinetics (col. 7, ll. 34-40) as the complex is formed in the liquid phase prior to being separated onto a solid phase.

Based on these teachings, Applicants respectfully submit that one of ordinary skill in the art, upon reading Jou, et al., would be led in a direction divergent from the path that was taken by Applicants. Specifically, the methods of Jou, et al. form a capture reagent/analyte/indicator reagent complex in solution, and then utilize a charged substance on a solid matrix to separate the complex (as well as unbound capture reagent) from the solution.

According to Jou, et al., the invention provides two major advancements, the first being the use of liquid phase kinetics to facilitate formation of a complex formed from the homogeneous mixture of analyte and assay reagent specific binding members, and the second being the potential number of complexes that can be immobilized on the solid support.

Thus, one of the *major advancements* of Jou, et al. is the utilization of liquid phase kinetics, i.e., all of the steps in forming the capture reagent/analyte/indicator

reagent complex are carried out in solution, which includes the step of binding the capture reagent to the analyte/indicator reagent. In contrast, the method of independent claim 37 requires a capture reagent in a detection zone. Thus, when utilizing the method of independent claim 37, the binding of the capture reagent to the conjugated probes will not take place in the liquid phase, but will take place in a dry chemistry format, with the capture reagent immobilized in the detection zone rather than in solution with the analyte and the other assay reagent specific binding members.

One of ordinary skill in the art, upon reading Jou, et al. would be led toward the solution chemistry format of Jou, et al., as the entire reference is directed to this format and the reference itself specifically teaches that this concept is a *major advancement to the field*. Accordingly, as one of skill in the art, upon reading Jou, et al., would be led in a direction divergent from the path that was taken by Applicant, it is respectfully maintained that the Examiner has failed to present a *prima facie* case of obviousness, as is required.

No common sense line of reasoning has been provided that would lead one of ordinary skill in the art from the teachings of Brooks, et al. to the suggested combination with Buck and Jou, et al. Only with Applicants' specification could the structure of independent claim 37 be attained, and any attempt to arrive at the structure of independent claim 37 through study of the cited references is only reachable from improper hindsight analysis after viewing Applicants' specification. In fact, the only teaching directed toward utilization of a polyelectrolyte as a capture reagent in a calibration zone is in the captioned application. Clearly, the only incentive or motivation for modifying Brooks, et al. using the teachings of Buck and Jou, et al. in the manner

suggested in the Office Action results from using Applicants' disclosure as a blueprint to reconstruct the claimed invention out of isolated teachings in the prior art, which is improper under *35 U.S.C. § 103*.

Of course, other distinctions also exist. Brooks, et al., for instance, describes a membrane strip that includes an application point, a contact region, and a detection zone. The contact region includes test particles coated with a binding agent for the analyte (e.g., an antibody) that can move through the strip and bind to a reagent in the detection zone. To provide an approximation of the amount of non-specific reaction of the test particles, the contact region also includes internal control particles coated with a binding agent that is *not specific* for the analyte. The internal control particles also move through the strip and can bind to a reagent in a control zone. However, the binding agent of the control particles is not specific for the analyte, such as an antibody that binds to an antigen that is uninvolved in the assay.

In Example 1 of Brooks, et al., for instance, the test particles are coated with a mouse monoclonal antibody that is specific for a myoglobin analyte. On the other hand, the internal control particles are coated with mouse monoclonal antibody MOPC31-c, which has an unknown specificity for myoglobin. According to Brooks, et al., the purpose of using such internal control particles, which are not specific for the analyte, is to determine the amount of "non-specific binding" that occurs during the assay. As correctly noted by the Examiner, however, Brooks, et al. fails to disclose numerous limitations of independent claim 37. For example, Brooks, et al. completely fails to disclose the claimed "scavenging zone."

The Office Action attempts to cure the deficiencies noted above by combining Brooks, et al. with Buck. Applicants note, however, excess analyte was not even a problem in Brooks, et al. Accordingly, one of ordinary skill in the art having common sense at the time of the invention would not have reasonably looked to Buck or any other reference to solve a problem that did not exist. Respectfully, the claimed invention taken as a whole is not obvious when considering the references in their entirety.

Regardless, even if the references are somehow combined, they still fail to disclose various features of the present claims. Dependent claim 41, for example, requires that the first capture reagent (scavenging zone) and the second capture reagent (detection zone) both include antibodies that bind to the same epitope of the analyte. Thus, should any of the first capture reagent somehow become free from the scavenging zone and travel to the detection zone, it will not bind to the second capture reagent and adversely impact the desired reduction in detection sensitivity. Neither Brooks, et al. nor Buck discloses this feature.

Thus, for at least the reasons indicated, Applicants respectfully submit that the present claims patentably define over the cited references, taken singularly or in any proper combination. It is believed that the present application is in complete condition for allowance and favorable action, therefore, is respectfully requested. Examiner DiRamio is invited and encouraged to telephone the undersigned, however, should any issues remain after consideration of this Amendment.

Please charge any additional fees required by this Amendment to Deposit Account No. 04-1403.

Respectfully requested,

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10/5/09
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